**MGMT Promoter Methylation Associated with Improved Survival for Patients with WHO Grade II Gliomas**

PHILADELPHIA, PA — Further exploration into the endpoints of the NRG Oncology/RTOG 0424 trial resulted in the discovery that *MGMT* promoter methylation is an independent prognostic biomarker of high-risk, low-grade glioma treated with temozolomide and radiation. This is the first study of its kind to validate the prognostic significance of *MGMT* promoter methylation in this patient population and treatment regimen. These findings were published in *JAMA Oncology* on June 28, 2018.

"*MGMT* promoter methylation has been known to represent a significant prognostic marker in Glioblastoma for over a decade, but its prognostic value had yet to be validated in High-Risk Low-Grade Glioma (LGG) patients. RTOG 0424 was the first study to prospectively validate MGMT promoter methylation in this setting, providing clinicians another tool to risk-stratify LGG patients moving forward," Stated Dr. Chakravarti.

The initial report on NRG Oncology/RTOG 0424 established a three-year survival benefit for patients with WHO grade II gliomas who received a combination of temozolomide and radiation. This analysis now provides overall survival and progression-free survival outcomes related to the MGMT promoter methylation. The study, designed using the MGMT-STOP27 prediction model to calculate *MGMT* promoter methylation status from Illumina HM-450K data, used univariate (UVAs) and multivariable analysis (MVAs) Cox proportional hazard models to determine the effect of *MGMT* status on survival outcomes.

Seventy-five of the 129 eligible trial participants from NRG Oncology/RTOG 0424 had *MGMT* status available. Fifty-seven (76.0%) of the patients with *MGMT* status available were methylated, whereas 18...
(24.0%) were unmethylated. Results substantiate that MGMT promoter methylation is correlated with progression-free survival and overall survival and should be incorporated into future clinical trial designs. NRG Oncology/RTOG 0424 was funded by the National Cancer Institute, Merck, and the Pennsylvania Department of Health. This project was supported by grants U10CA180868 (NRG Oncology Operations), U10CA180822 (NRG Oncology SDMC), U24CA196067 (NRG Specimen Bank) from the National Cancer Institute (NCI) and Merck. This project is funded, in part, under a grant with the Pennsylvania Department of Health. The Department specifically disclaims responsibility for any analyses, interpretations, or conclusions. Also, R01CA108633, R01CA169368, RC2CA148190, U10CA18085001 from the NCI, Brain Tumor Funders Collaborative Grant, and The Ohio State University CCC (all to AC).

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NRG Oncology conducts practice-changing, multi-institutional clinical and translational research to improve the lives of patients with cancer. Founded in 2012, NRG Oncology is a Pennsylvania-based nonprofit corporation that integrates the research of the NSABP Foundation, the Radiation Therapy Oncology Group (RTOG), and the Gynecologic Oncology Group (GOG). The research network seeks to carry out clinical trials with emphases on gender-specific malignancies, including gynecologic, breast, and prostate cancers, and on localized or locally advanced cancers of all types. NRG Oncology’s extensive research organization comprises multidisciplinary investigators, including medical oncologists, radiation oncologists, surgeons, physicists, pathologists, and statisticians, and encompasses more than 1,300 research sites located world-wide with predominance in the United States and Canada. NRG Oncology is supported primarily through grants from the National Cancer Institute (NCI) and is one of five research groups in the NCI’s National Clinical Trials Network.